United States Court of Appeals for the Federal Circuit

02-1492

GLAXO GROUP LTD.
and SMITHKLINE BEECHAM CORPORATION,

Plaintiffs-Appellees,

v.

APOTEX, INC.,

Defendant-Appellant.

DECIDED: April 22, 2003

Before MICHEL, CLEVENGER, and SCHALL, Circuit Judges.

MICHEL, Circuit Judge.

Defendant Apotex, Inc. appeals the June 10, 2002, order of the United States District Court for the Northern District of Illinois, Glaxo Group Ltd. v. Apotex, Inc., No. 00-CV-5791 (N.D. Ill. June 10, 2002), preliminarily enjoining Apotex from marketing a generic antibiotic drug, cefuroxime axetil ("CA"), that allegedly infringes U.S. Pat. Nos. 4,562,181 ("the '181 patent") and 4,820,833 ("the '833 patent"), owned by plaintiffs Glaxo Group Ltd. and Smithkline Beecham Corp. (collectively "GSK"). Because on this record, in the preliminary injunction context, the district court did not err in construing

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the patent claim "purity" as excluding excipients from being considered impurities, and did not abuse its discretion in entering the preliminary injunction, we affirm.

BACKGROUND

Because we write solely for the benefit of those involved, especially appellant, we recount the facts and procedural history of the case only insofar as they are material to our analysis, which follows.

Both the '181 and '833 patents are directed to a highly pure, substantially amorphous form of CA. The '181 patent covers the product itself, while the '833 patent covers a process for preparing such CA. Because the '833 patent expired on December 31, 2002 due to a terminal disclaimer, we need only address issues relating to the '181 patent.

Claims 1 and 8 of the '181 patent read:

> 1. Cefuroxime axetil in amorphous form essentially free from crystalline material, and having a purity of at least 95% aside from residual solvents.
>
> 8. An antibacterial pharmaceutical composition containing an antibacterially effective amount of cefuroxime axetil according to claim 1 in admixture with one or more pharmaceutical carriers or excipients.

'181 patent, col. 13, ll. 4-6 and col. 14, ll. 1-4. The '181 patent claims a highly pure CA in amorphous form because the patentee discovered that "contrary to previous experience in the cephalosporin field," highly pure CA in amorphous form has better bioavailability upon oral administration compared to highly pure CA in crystalline form. Id. col. 2, ll. 7-15. "This is despite the known tendency for amorphous materials to have inferior chemical stability to crystalline materials and also the known tendency for highly pure amorphous materials to crystallize." Id. col. 2, ll. 15-18. The specification thus discloses:

> According to one aspect of the present invention, there is provided cefuroxime axetil in highly pure, substantially amorphous form.
>
> The cefuroxime axetil in accordance with the invention preferably contains less than 5% mass/mass (m/m), advantageously less than 3% m/m, of impurities. It is to be understood that references herein to 'impurities' are to be understood as not including residual solvents remaining from the process used in the preparation of the cefuroxime axetil of the invention. . . .
>
> Typical impurities which may be present are the Δ2-isomers of cefuroxime axetil and the corresponding E-isomers of cefuroxime axetil.

Id. col. 2, ll. 27-38.

As initially filed, claim 1 read: "Cefuroxime axetil in highly, pure, substantially amorphous form." Upon the Examiner's indefiniteness rejection, the claim was changed to "Cefuroxime axetil in amorphous form essentially free from crystalline material, which contains less than 5% m/m of impurities other than residual solvents and less than 6% m/m of residual solvents." Upon another rejection based on § 112, ¶¶ 1 and 2, Glaxo changed the claim to the current form and eliminated the reference to "impurities." All of remaining claims were then allowed.

Glaxo holds the New Drug Application for CA tablets sold under the brand name Ceftin. In May 2002, Glaxo moved to preliminarily enjoin Apotex from selling its generic CA product after being informed that approval by the Food and Drug Administration ("FDA") of Apotex's abbreviated new drug application ("ANDA") was imminent. The district court held a hearing in June, and later entered the preliminary injunction. The court set the bond at $5 million, although Apotex sought a bond of at least $40 million.

The FDA approved Apotex's ANDA on October 2, 2002. Apotex moved for an increase in the bond to more than $162 million. The district court required an additional $3 million in the amount of the bond.

On appeal Apotex challenges the district court's claim construction, its preliminary injunction decision based on its findings of GSK's likelihood of success on the merits with respect to infringement and validity and the other balancing factors, and the amount of bond.

DISCUSSION

We review a trial court's decision on a preliminary injunction to determine "whether the district court abused its discretion, committed an error of law, or seriously misjudged the evidence underlying its findings of fact." Nutrition 21 v. United States, 930 F.2d 867, 869, 18 USPQ2d 1347, 1349 (Fed. Cir. 1991). We review a district court's legal conclusions such as claim construction de novo. Novo Nordisk of N. Amer., Inc. v. Genentech, Inc., 77 F.3d 1364, 1368, 37 USPQ2d 1773, 1776 (Fed. Cir. 1997).

Apotex contends that (I) the district court erred in its claim construction, (II) Glaxo did not prove likelihood of success on infringement, (III) Apotex raised a substantial question with respect to the validity of the patent, (IV) Glaxo did not meet its burden of showing irreparable harm and the other factors for a preliminary injunction, and (V) the district court abused its discretion in setting the amount of the bond. After considering each of Apotex's arguments, we conclude that, in the preliminary injunction context, the district court did not err in its claim construction, Glaxo proved likelihood of success on infringement, Apotex did not raise a substantial question regarding the validity of the '181 patent, and the court did not abuse its discretion in granting a preliminary injunction or setting the amount of bond.

I

Apotex argues that the district court erred in construing claim 1 of the '181 patent as covering CA having no more than 5% degrading, unwanted impurities not including excipients, such as the sorbitol and zinc chloride added by Apotex to its CA product. Apotex asserts that "a purity of at least 95%" means at least 95% of a sample has to be CA regardless of what the remaining 5% is.

The district court did not commit legal error in claim construction in its preliminary injunction decision. First, to read the CA of claim 1 as containing less than 5% of anything other than CA would read preferred embodiments of the invention out of the scope of the claim. For example, the product disclosed in Example 26 contains 60% of CA and 40% of additives. '181 patent, col. 11, ll. 42-55. It is well established that claims are generally construed so as to not exclude a preferred embodiment. See Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1583, 39 USPQ2d 1573, 1578 (Fed. Cir. 1996) (stating that a claim interpretation that excluded a preferred embodiment "is rarely, if ever, correct and would require highly persuasive evidentiary support, which is wholly absent in this case"). Second, the specification describes impurities and that the typical impurities are degrading, unwanted isomers of CA. '181 patent, col. 2, ll. 27-38. The description of the typical impurities in the specification is consistent with the patentee's early attempt during the prosecution history to define the invention using a percentage of impurities.

We thus conclude that, in the context for the preliminary injunction, the district court did not err in construing claim 1 so that excipients would not be counted as impurities to affect the purity of CA as claimed by the '181 patent. Although GSK and

Apotex also dispute various dictionary definitions of "purity," we find the district court's construction correct at least for purposes of a preliminary injunction in view of the claims, specification, and prosecution history of the '181 patent.

II

"[B]ecause of the extraordinary nature of the relief, the patentee carries the burden of showing likelihood of success on the merits with respect to the patent's validity, enforceability, and infringement." Novo Nordisk, 77 F.3d at 1367, 37 USPQ2d at 1775. Apotex argues that GSK did not prove likelihood of success on infringement because Apotex's CA product is an amorphous co-precipitate, not "cefuroxime axetil in amorphous form," and Apotex's co-precipitate does not satisfy the "purity of at least 95%" claim limitation.

Although claim construction is a question of law, infringement, either literal or under the doctrine of equivalents, is a question of fact. Bai v. L & L Wings, Inc., 160 F.3d 1350, 1353, 48 USPQ2d 1674, 1676 (Fed. Cir. 1998). We conclude that the district court did not clearly err in finding that GSK proved likelihood of success with respect to infringement. The court did not clearly err in finding that there was no chemical difference between Apotex's co-precipitate created by mixing pure CA and the excipients into acetone and then spray-drying it to make it amorphous, and GSK's patented product created by mixing pure CA in acetone and spay-drying it to make it amorphous and then combining the result with excipients. Although CA is air-dried together with excipients to form Apotex's product, it is not asserted that the air-drying process changes the chemical properties of CA. The claims of the '181 patent do not require that amorphous CA be in certain separable particles or a certain phase. Thus,

the CA in Apotex's co-precipitate is still CA after the drying process, and the CA is amorphous after the drying even though it co-exists in such form with the excipient molecules. Additionally, the district court did not clearly err in finding that Apotex's products satisfied the "purity of at least 95%" claim limitation because it is undisputed that, excluding excipients, Apotex's CA is at least 95% pure.

Further, for the same reasons stated above, the district court did not clearly err in finding that claim 8, as well as claim 1, is likely infringed.[1]

III

Apotex also argues that it raised a substantial question with respect to the validity of the patents in suit. Apotex asserts that its expert, Dr. Siegel, followed the teachings of a prior art patent, U.S. Pat. No. 4,264,320 ("the '320 patent"), and found that the CA obtained was inherently amorphous and had a purity greater than 97%. Thus, Apotex asserts, the invention claimed in the '181 patent is anticipated by the '320 patent. Apotex asserts obviousness as well, which is based on anticipation, except claims 6 and 12, which are allegedly obvious because of an expert declaration of obviousness.

We conclude that the district court did not clearly err in finding that Apotex failed to raise a substantial question concerning validity of the '181 patent. There is no clear error in the court's findings that Dr. Siegel did not follow Example 1 of the '320 patent precisely but instead elected to mix other methods from other portions of the patent to

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[1] Apotex also relies on a Canadian federal court decision finding that the Canadian equivalent to the '181 patent was not infringed by Apotex's CA product. We note that the Canadian judgment construing the Canadian patent and applying Canadian patent law does not control our decision here.

come up with a highly pure, amorphous CA, and that Apotex failed to present persuasive evidence to show that one skilled in the art would have selected the particular elements from the '320 patent as selected by Dr. Siegel and come up with the product claimed by the '181 patent. The district court thus did not clearly err in finding that Apotex failed to raise a substantial question on anticipation. Neither did it clearly err in finding that Apotex failed to present persuasive evidence that the subject matter of the '181 patent would have been obvious at the time the invention was made to a person having ordinary skill in the art.

IV

Apotex further argues that GSK did not prove the other factors relevant to a preliminary injunction, but rather that factors such as irreparable harm, balancing of hardships, and the public interest should be so decided as to warrant denying the preliminary injunction. After considering the district court's findings relevant to each factor, we do not see clear error.

(1) Irreparable harm

Apotex argues that the district court committed legal error in presuming that GSK would sustain irreparable harm, and that GSK did not meet its burden of showing irreparable harm.

A presumption of irreparable harm arises upon a clear (or strong) showing of infringement and validity. Roper Corp. v. Litton Sys., Inc., 757 F.2d 1266, 1271, 225 USPQ 345, 348 (Fed. Cir. 1985). Here, although the district court did not expressly state that there was a clear showing of infringement and validity, it seemed to have found so. Even if the presumption does not apply for a lack of clear showing of

infringement and validity, we conclude that the court did not clearly err in finding that such irreparable harm was likely to occur. There is ample evidence in the record to show that allowing Apotex to market its generic CA product would cause unquestionable loss of GSK's patent right, in view of GSK's likelihood of success with respect to infringement and validity. Although Apotex presented an expert declaration that a brand name would maintain its price rather than suffer lowering of its prices upon generic entry, GSK on the other hand has shown that generic entry, even if it is not the first generic competition, would affect not only price and profit but also cause a significant loss in market share.

(2) Balance of hardships

Apotex also argues that a balancing of the hardships favors Apotex because it faces greater harm from being kept off the market than GSK would have faced without the injunction. Apotex asserts that after the huge amount of investment it put into preparing to bring the generic CA to the market, it stands to lose millions of dollars a month as a result of the delay in the market entry. GSK, on the other hand, has already enjoyed many years of monopoly sales for Ceftin, and already faces generic competition from the first generic competition, Ranbaxy.

The district court did not clearly err in finding that, without the preliminary injunction, Glaxo would lose the value of its patent while Apotex would only lose the ability to go on to the market and begin earning profits earlier. Additionally, Apotex's loss of profit is secured by the issuance of the bond if the ultimate ruling is non-infringement or patent invalidity. The court did not clearly err in finding that additional generic competition would likely drive down the brand name's price and market share,

causing permanent loss of customers and users of plaintiffs' patented product. Thus, the court did not abuse its discretion in finding that a balancing of the hardships favored the patentee GSK.

(3) Public interest

Finally, the district court did not clearly err in finding that public interest favors the patentee as the court found that the value of patent protection for the patent's full term was more important in this case than allowing a second generic Ceftin maker to enter the market early. To the extent that the public interest favors generic competition, it is also the public's strong interest to protect patent rights, especially in view of GSK's likelihood of success with respect to infringement and validity of the patent.

V

Apotex repeatedly argues both at the district court level and on appeal that the bond set by the district court should be raised.

We do not find that the district court abused its discretion in setting a bond at $5 million and then raising it to $8 million after the FDA approved Apotex's ANDA in October 2002. The '181 patent will expire only about ten months after the FDA approval. There is already another generic Ceftin maker on the market. Apotex has not provided sufficient evidence to support a higher amount for the bond, or show how the trial court abused its discretion here.

CONCLUSION

We hold that at the preliminary injunction setting, the district court did not err in construing the claims of the '181 patent as excluding excipients from impurities in calculating the purity of the CA. Additionally, the district court did not clearly err in

finding GSK's likelihood of success with respect to infringement and validity. Further, the court did not clearly err in its findings on irreparable harm, balancing of hardships and public interest. The court did not abuse its discretion in granting a preliminary injunction. Nor did it abuse its discretion in setting the amount of bond. Accordingly, the order of the district court is, in all respects challenged on appeal, affirmed.